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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,040	10/03/2003	Mitchell P. Fink	3258.1000-004	1662

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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/679,040	FINK ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 20-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 20-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/08/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. By Amendment filed 08/16/2006, claims 19 and 27-30 have been cancelled and claim 1 has been amended.

2. Claims 1-18 and 20-26 are currently pending for prosecution on the merits.

Summary of Action

3. The rejection of claims 1-30 under 35 U.S.C. 103(a) as being unpatentable over Nath (USP 5,210,098) in view of DiPiro (Pharmacotherapy, A Pathophysiologic Approach, pp. 515-24, 1989) and Solomons, T.W. (Organic Chemistry, 3rd Edition, pages 794-797 and 814-815, 1984) is maintained for the reasons of record.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-18 and 20-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nath (USP 5,210,098) in view of DiPiro (Pharmacotherapy, A Pathophysiologic Approach, pp. 515-24, 1989) and Solomons, T.W. (Organic Chemistry, 3rd Edition, pages 794-797 and 814-815, 1984).

Nath teaches that pyruvate salt, including sodium pyruvate as well as other nontoxic alkali metal and alkaline earth metal salts of pyruvic acid may be utilized in the treatment of acute renal failure. (see abstract and column 2, lines 13-16 and column 6, lines 57-60). Nath also teach it is known in the art that alpha-keto acids may be efficacious in retarding the progression of established renal disease, (see column 1, lines 38-42). Nath teaches the skilled artisan of pyruvate and alph-keto acids exert cytoprotection against peroxide induced oxidant stress, (see column 3, lines 3-5 and lines 21-30).

DiPiro teaches that acute renal failure has various etiologies, such as diminished renal blood flow, obstruction of urine flow, and reduction in glomerular filtration rate, (see page 515). DiPiro also teach of the administration of other various agents to treat acute renal failure, such as mannitol, dopamine, furosemide, as well as monitoring fluid and electrolyte balance, such as

calcium, and restriction protein intake, (see page 520). DiPir0 disclose that cardiovascular complications that may occur with acute renal failure include hypertension, hypotension, cardiac failure, arrhythmias, (see page 522). It would have been obvious to the skilled artisan to recognize, determine, diagnosis risk factors of acute renal failure, such as various causes of decreased renal blood flow, cardiovascular complications, and metabolic disorders and be able to treat and prevent the development of additional complications of renal failure. Also, the skilled artisan would recognize that various pharmaceutical agents could be combined to treat various symptoms and functions of acute renal failure. The difference between the prior art and that of the instantly claimed subject matter is with respect to the carboxylic acid/salt moiety of the alpha-keto acid, such as pyruvate, and the claimed carboxylic acid ester moiety, namely ethyl pyruvate. It is well within the purview of the skilled artisan to recognize, determine, and synthesize a carboxylic acid ester or carboxylic acid amide from the corresponding carboxylic acid/salt moiety. One having ordinary Skill in organic and medicinal chemistry could easily convert from a carboxylic acid or a carboxylic acid salt into the corresponding carboxylic acid ester group by simply reacting the carboxylic acid moiety with a alcoholic group, such as ethanol, benzyl alcohol, polyol, sugar, or in the case of obtaining the carboxylic acid amide, reacting the carboxylic acid group with an amine compound, (see reaction 7 on page 815 of Solomons, T.W). In addition, one having ordinary skill in the art would be motivated from the prior art teachings of Nath, which is directed to the administration of the alpha-keto acid, such as pyruvate, for the treatment of acute renal failure, and arrive at the instantly claimed subject matter of treating the very same ailment but now with the corresponding derivative of a carboxylic acid, in the case of Nath the carboxylic acid salt, which is the carboxylic acid ester.

Clearly, one having ordinary skill in the art would have been motivated with the explicit teachings of Nath to use an alpha-keto acid, such as pyruvate, and change it into the corresponding ester or amide derivatives of a carboxylic acid, which embraces the claimed carboxylic acid esters and amides of the claimed subject matter.

Response to Arguments

5. Applicant's arguments filed 08/16/2006 have been fully considered but they are not persuasive.

Applicant's argument in the response takes the position that neither Nath, DiPiro or solomons alone or in combination teaches or suggests provide any suggestion of the use of a pyruvate ester in the treatment of acute renal failure, nor the administration of a pyrvate ester that would be advantageous or effective in the treatment of acute renal failure. Applicant alleges that in the absence of any teaching that a pyruvate ester would be beneficial or even effective in treating acute renal failure, one of ordinary skill would have had no motivation to substitute in the pyrvate salt taught by Nath with a pyruvate ester of the present claims.

This argument is not found persuasive. Unlike the applicant's argument, one having ordinary skill in the art would have been motivated to select the claimed ester compound with the expectation that ester or amide analogues of 2-ketoalkanoic acid would have similar activity as the salt of 2-ketoalkanoic acid due to close structural similarity of the compounds (see USP 4380549, USP 2005/0197397, USP 6943190, and USP 5294641).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching,

suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. No Claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
Primary Patent Examiner
AU 1614